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PATENT  
Docket No. 120-243

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

MARCUS A. HORWITZ ET AL.

Serial No.: 08/786,533

: Art Unit: 1802

Filed: January 21, 1997

: Examiner: Rodney P. Swartz, Ph.D.

For: ABUNDANT EXTRACELLULAR PRODUCTS AND  
METHODS FOR THEIR PRODUCTION AND USE

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

This Information Disclosure Statement is being filed before the mailing date of the first Office Action issued on the merits of the above-identified application in accordance with 37 C.F.R. § 1.97(b)(3).

In recognition of Applicants' duty to inform the U.S. Patent and Trademark Office of relevant patents, publications, or other information of which Applicants are aware, Applicants have enclosed herewith copies of the Information Disclosure Statements that were submitted in the following parent applications of the above-identified application: Serial No. 08/156,358 filed

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November 23, 1993; Serial No. 08/289,667 filed August 12, 1994; Serial No. 08/447,398 filed May 23, 1995; Serial No. 08/551,149 filed October 31, 1995; Serial No. 08/568,357 filed December 6, 1995 and Serial No. 08/652,842 filed May 23, 1996. Where duplicate Information Disclosure Statements were submitted to more than one of the prior applications, only one copy of such Information Disclosure Statement from one of the prior applications is enclosed.

This application relies, under 35 U.S.C. § 120, on the earlier filing dates of these prior applications. The identified references were submitted to the U.S. Patent Office in these prior applications and, therefore, are not required to be provided in this application pursuant to 37 C.F.R. § 1.98(d). However, if the Examiner requests, Applicants will provide additional copies of the references that are listed in these prior Information Disclosure Statements.

The filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made, as an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

It is believed that this Information Disclosure Statement does not require any fee. However, the Commissioner is authorized to charge any fee which may be required in connection with this paper to deposit account No. 16-2230. A duplicate copy of this paper is enclosed for this purpose.

Respectfully submitted,

Dated: March 13, 1997

  
\_\_\_\_\_  
Kurt A. MacLean  
Registration No. 31,118  
Attorney for Applicants

**OPPENHEIMER POMS SMITH**  
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FILE COPY

PATENT  
Docket No. 115-066

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Tina Carlin

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

MARCUS A. HORWITZ

Serial No.: 08/568,357

: Art Unit: n/a

Filed: December 6, 1995

: Examiner: n/a

For: ABUNDANT EXTRACELLULAR PRODUCTS AND  
METHODS FOR THEIR PRODUCTION AND USE

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

This Information Disclosure Statement is being filed before the mailing date of the first Office Action issued on the merits of the above-identified application in accordance with 37 C.F.R. § 1.97(b)(3), and supplements the Information Disclosure Statements previously filed on April 9, 1996, for this application.

In recognition of Applicant's duty to inform the U.S. Patent and Trademark Office of relevant patents, publications, or other information of which Applicant is aware, Applicant submits herewith copies of the following references relating to *Mycobacterium tuberculosis*

extracellular proteins which may be material to the examination of the above-identified application.

- ✓ 1. Allison, A. C., and N. E. Byars. "An Adjuvant Formulation That Selectively Elicits the Formation of Antibodies of Protective Isotypes and of Cell-Mediated Immunity." *Journal of Immunological Methods* 95 (1986) 157-68.
- ✓ 2. Andersen, P., and I. Heron. "Specificity of a Protective Memory Immune Response against *Mycobacterium tuberculosis*." *Infection and Immunology* 61 (1993) 844-51.
- ✓ 3. Belisle, J. T., et al. "Identification of a Mycolyltransferase from *Mycobacterium tuberculosis* and the Coincident Definition of the Physiological Function of Antigen 85B." In the program from the *Thirtieth U.S.-Japan Tuberculosis Research Conference, Leprosy Research Conference and Tuberculosis/Leprosy Symposium*. U.S.-Japan Cooperative Medical Science Program. Ft. Collins, Colorado (July 19-21, 1995) 212-6.
- ✓ 4. Chen, E. Y., and P. H. Seeburg. "Supercoil Sequencing: A Fast and Simple Method for Sequencing Plasmid DNA." *DNA* 4 (1985) 165-70.
- ✓ 5. Clemens, D. L., and M. A. Horwitz. "Characterization of the *Mycobacterium tuberculosis* Phagosome and Evidence That Phagosomal Maturation Is Inhibited." *Journal of Experimental Medicine* 181 (1995) 257-70.
- ✓ 6. Feller, D. C., and V. F. de la Cruz. "Identifying Antigenic T-Cell Sites." *Nature* 349 (1991) 720-1.
7. Grunstein, M., and D. S. Hogness. "Colony Hybridization: A Method for the Isolation of Cloned DNAs That Contain a Specific Gene." *Proceedings of the National Academy of Science USA* 72 (1975) 3961-6.
- ✓ 8. Harth, Günter, et al. "Glutamine Synthetase of *Mycobacterium tuberculosis*: Extracellular Release and Characterization of Its Enzymatic Activity." *Proceedings of the National Academy of Science USA* 91 (1994) 9342-6.
- ✓ 9. Hatfull, G. F., and G. J. Sarkis. "DNA Sequence, Structure and Gene Expression of Mycobacteriophage L5: A Phage system for Mycobacterial Genetics." *Molecular Microbiology* 7 (1993) 395-405.

- ✓ 10. Huygen, Kris, et al. "Specific Lymphoproliferation, Gamma Interferon Production, and Serum Immunoglobulin G Directed against a Purified 32 kDa Mycobacterial Protein Antigen (P32) in Patients with Active Tuberculosis." *Scandinavian Journal of Immunology* 27 (1988) 187-94.
11. Kitaura, H., et al. "Cloning, Sequencing and Expression of the Gene for Alpha Antigen from *Mycobacterium intracellulare* and Use of PCR for the Rapid Identification of *Mycobacterium intracellulare*." *Biochemical and Biophysical Research Communications* 196 (1993) 1466-73.
12. Kremer, L., et al. "Analysis of the *Mycobacterium tuberculosis* 85A Antigen Promoter Region." *Journal of Bacteriology* 177 (1995) 642-53.
13. Kyte, J., and R. F. Doolittle. "Simple Method for Displaying the Hydropathic Character of a Protein." *Journal of Molecular Biology* 157 (1982) 105-32.
14. Launois, P., et al. "T-Cell-Epitope Mapping of the Major Secreted Mycobacterial Antigen Ag85A in Tuberculosis and Leprosy." *Infection and Immunity* 62 (1994) 3679-87.
15. Lee, B.-Y., and M. A. Horwitz. "Identification of Macrophage and Stress-Induced Proteins of *Mycobacterium tuberculosis*." *Journal of Clinical Investigation* 96 (1995) 245-9.
- ✓ 16. Lee, T. D., and S. Vemuri. "MacProMass: A Computer Program to Correlate Mass Spectral Data to Peptide and Protein Structures." *Biomedical and Environmental Mass Spectroscopy* 19 (1990) 639-45.
17. Matsuo, K., et al. "Cloning and Expression of the *Mycobacterium bovis* BCG Gene for Extracellular  $\alpha$  Antigen." *Journal of Bacteriology* 170 (1988) 3847-54.
18. Pribnow, D. "Nucleotide Sequence of an RNA Polymerase Binding Site at an Early T7 Promoter." *Proceedings of the National Academy of Science USA* 72 (1975) 784-8.
19. Sanger, F., et al. "DNA Sequencing with Chain-Terminating Inhibitors." *Proceedings of the National Academy of Science USA* 74 (1977) 5463-7.

✓ 20. Shine, J., and L. Dalgarno. "The 3'-Terminal Sequence of *Escherichia coli* 16S Ribosomal RNA: Complementarity to Nonsense Triplets and Ribosome Binding Sites." *Proceedings of the National Academy of Science USA* 71 (1974) 1342-6.

✓ 21. Shinnick, T. M. "The 65-Kilodalton Antigen of *Mycobacterium tuberculosis*." *Journal of Bacteriology* 169 (1987) 1080-8.

✓ 22. Yanisch-Perron, C., et al. "Improved M13 Phage Cloning Vectors and Host Strains: Nucleotide Sequences of the M13mpl8 and pUC19 Vectors." *Gene* 33 (1985) 103-19.

✓ 23. Von Heijne, G. "A New Method for Predicting Signal Sequence Cleavage Sites." *Nucleic Acids Research* 14 (1986) 4683-90.

All of the above references are also listed on the attached PTO Form-1449.

In filing this Information Disclosure Statement, Applicant notes that none of the references listed above discloses the use of majorly abundant extracellular products to induce protective immunity to subsequent infection by intracellular pathogens.

The filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made, as an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

It is believed that this paper does not require any fee. However, the Commissioner is authorized to charge any fee which may be required in connection with this paper to deposit account No. 16-2230. A duplicate copy of this paper is enclosed for this purpose.

Respectfully submitted,

Dated: April 19, 1996

  
Kurt A. MacLean

Kurt A. MacLean  
Registration No. 31,118  
Attorney for Applicant

POMS, SMITH, LANDE & ROSE  
Professional Corporation  
2029 Century Park East, Suite 3800  
Los Angeles, California 90067  
(714) 263-8250

I certify that on November 14, 1994, which is the date I am signing this certificate, this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.



Tina Carlin

Tina Carlin  
November 14, 1994

**COPY**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

MARCUS A. HORWITZ

Serial No.: 08/289,667

Filed: August 12, 1994

For: ABUNDANT EXTRACELLULAR  
PRODUCTS AND METHODS FOR  
THEIR PRODUCTION AND USE

Group Art Unit:

Examiner:

Docket No.: 104-223

PERTINENT INFORMATION DISCLOSURE STATEMENT

BOX DD  
Commissioner of Patents  
and Trademarks  
Washington, D. C. 20231

Dear Sir:

Enclosed herewith is a copy of the Pertinent Information Disclosure Statement that was submitted in the parent application, Serial No. 08/156,358, filed November 23, 1993. Copies of the references listed in such statement were submitted in the parent application.

I certify that on May 15, 1995, which is the date I am signing this certificate, this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Tina Carlin  
Tina Carlin  
May 15, 1995

**COPY**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of	:	Group Art Unit: 1806
MARCUS A. HORWITZ	:	Examiner:
Serial No.: 08/289,667	:	
Filed: August 12, 1994	:	
For: ABUNDANT EXTRACELLULAR PRODUCT	:	
VACCINES AND METHODS FOR THEIR	:	
PRODUCTION AND USE	:	
	:	Atty. Docket No. 104-223

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
FILED BEFORE MAILING OF FIRST OFFICE ACTION

Commissioner of Patents  
and Trademarks  
Washington, D.C. 20231

Sir:

In recognition of Applicant's duty to inform the Patent Office of relevant patents, publications or other information of which Applicant is aware, Applicant has enclosed the patents and publication as set forth in the attached form PTO-1449.

The filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made, an admission that the information cited is, or is considered to be, material to patentability or that no other material information exists.

The filing of this Information Disclosure Statement shall not be construed as an admission against interest in any matter.

This application relies, under 35 USC Section 120, on the earlier filing date of prior application Serial No. 08/156,358, filed on November 23, 1993. The identified references were submitted to the Patent Office in the prior application and, therefore, are not required to be provided in this application pursuant to 37 CFR Section 1.98(d).

The attached references are relevant in showing diagnostic skin tests for and vaccines against tuberculosis.

This supplemental Information Disclosure Statement is being filed before the mailing date of a first Official Action on the merits. Accordingly, no certification or fee is due, and the Examiner is respectfully requested to consider the attached references. If any additional fees are seen as being necessary in connection with this Information Disclosure Statement, please consider this to be a request therefore and charge Deposit Account No. 16-2230. A duplicate copy of this sheet is enclosed for that purpose.

Respectfully submitted,



Kurt A. MacLean  
Reg. No. 31,118  
Attorney for Applicant

May 15, 1995

KAM/tmc  
Enclosures

POMS, SMITH, LANDE & ROSE  
2029 Century Park East  
38th Floor  
Los Angeles, California 90067  
Telephone: (714) 263-8250

I certify that on January 24, 1996, which is the date I am signing this certificate, this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

*Tina Carlin*

Tina Carlin  
January 24, 1996

**COPY**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Group Art Unit:
MARCUS A. HORWITZ	)	Examiner:
Serial No.: 08/551,149	)	
Filed: October 31, 1995	)	
For: ABUNDANT EXTRACELLULAR PRODUCT VACCINES AND METHODS FOR THEIR PRODUCTION AND USE	)	Docket No.: 112-272

INFORMATION DISCLOSURE STATEMENT

Commissioner of Patents  
and Trademarks  
Washington, D. C. 20231

Dear Sir:

In recognition of Applicant's duty to inform the Patent Office of relevant patents, publications or other information of which Applicant is aware, Applicant has enclosed herewith copies of the Information Disclosure Statements that were submitted in the parent applications of the above-identified application, Serial No. 08/156,358 filed November 23, 1993, Serial No. 08/289,667 filed August 12, 1994, and Serial No. 08/447,398 filed May 23, 1995.

This application relies, under 35 U.S.C. § 120, on the earlier filing dates of these prior applications. The identified references were submitted to the Patent Office in these prior applications and, therefore, are not required to be provided in this application pursuant to 37 C.F.R. § 1.98(d). However, if the Examiner requests, Applicant will provide additional copies of the references that are listed in these prior information disclosure statements.

In addition to the previously cited references, Applicant is providing two additional references identified in the attached form PTO-1449. These references are relevant in showing molecular mechanisms in Tuberculosis and various species of *Mycobacterium* in addition to the characterization of secretory products thereof.

This Information Disclosure Statement is being filed within the three months of the application filing date. Accordingly, no certification or fee is due. However, if any additional fees are seen as being necessary in connection with this Information

Disclosure Statement, please charge deposit Account No. 16-2230.  
A duplicate copy of this sheet is enclosed for this purpose.

Respectfully submitted,



Kurt A. MacLean  
Reg. No. 31,118  
Attorney for Applicant

KAM/tmc  
Enclosures

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Facsimile: (714) 263-8260

I certify that on September 13, 1995, which is the date I am signing this certificate, this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231.

*Tina Carlin*

Tina Carlin  
September 13, 1995

**COPY**

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	)	Group Art Unit:
MARCUS A. HORWITZ	)	Examiner:
Serial No.: 08/447,398	)	
Filed: May 23, 1995	)	
For: ABUNDANT EXTRACELLULAR PRODUCTS AND METHODS FOR THEIR PRODUCTION AND USE	)	Docket No.: 111-161

INFORMATION DISCLOSURE STATEMENT  
FILED BEFORE MAILING OF FIRST OFFICE ACTION

BOX DD  
Commissioner of Patents  
and Trademarks  
Washington, D. C. 20231

Dear Sir:

In recognition of Applicant's duty to inform the Patent Office of relevant patents, publications or other information of which Applicant is aware, Applicant has enclosed herewith a copy of the Pertinent Information Disclosure Statement that was submitted in the parent applications of the above-identified application, Serial No. 08/156,358 filed November 23, 1993, and Serial No. 08/289,667

filed August 12, 1994, and a copy of the Supplemental Information Disclosure Statement Filed before Mailing of First Office Action that was submitted in Serial No. 08/289,667.

This application relies, under 35 U.S.C. § 120, on the earlier filing date of prior application Serial No. 08/156,358, filed on November 23, 1993. The identified references were submitted to the Patent Office in the prior application and, therefore, are not required to be provided in this application pursuant to 37 C.F.R. § 1.98(d). However, if the Examiner requests, Applicant will be happy to provide additional copies of the references that are listed in these prior information disclosure statements.

This Information Disclosure Statement is being filed before the mailing date of a first official Action on the merits. Accordingly, no certification or fee is due. However, if any additional fees are seen as being necessary in connection with this Information Disclosure Statement, please charge deposit Account No. 16-2230. A duplicate copy of this sheet is enclosed for this purpose.

Respectfully submitted,



Kurt A. MacLean  
Registration No. 31,118  
Attorney for Applicant

Enclosures

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Los Angeles, California 90067-3024  
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## PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:

MARCUS A. HORWITZ

Serial No.: 08/156,358

Date Filed: November 23, 1993

For: ABUNDANT EXTRACELLULAR  
PRODUCT VACCINES AND METHODS  
FOR THEIR PRODUCTION AND USE

Examiner: J. STAPLES

Art Unit: 1806

PERTINENT INFORMATION  
DISCLOSURE STATEMENT

Docket No.: 98-080

COPY

Box DD  
Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Dear Sir:

In recognition of Applicant's duty to inform the Patent Office of relevant patents, publications or other information of which Applicant is aware, Applicant has enclosed the documents as set forth in the attached form PTO-1449.

The filing of this Information Disclosure Statement shall not be construed as a representation that an independent search has been made (37 C.F.R. 1.97(g)), an admission that the information cited is, or considered to be, material to patentability or that no other material information exists.

No additional fees are seen as necessary at this time. If any additional fee or extension fee is required, this is the request therefor and to charge Account No. 16-2230. A duplicate of this transmittal letter is enclosed for that purpose.

Respectfully submitted,

Kurt A. MacLean  
Reg. No. 31,118  
Attorney for Applicant

May 25, 1994

POMS, SMITH, LANDE & ROSE  
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Executed on May 25, 1994

Frances E. Thorsen

If the Examiner requests, applicant will be happy to provide additional copies of the references that are listed in the prior Pertinent Information Disclosure Statement.

Respectfully submitted,



Kurt A. MacLean  
Attorney for Applicant  
Registration No. 16,960

KAM/tmc  
Enclosure

POMS, SMITH, LANDE & ROSE  
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Docket No. 98-080

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Tina Carlin

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re application of

MARCUS A. HORWITZ

Serial No.: 08/156,358

: Art Unit: 1802

Filed: November 23, 1993

: Examiner: Julie Krsek Staples, Ph.D.

For: PROTEIN VACCINE AGAINST TUBERCULOSIS  
AND OTHER INTRACELLULAR PATHOGENS

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT**

Commissioner of Patents and Trademarks  
Washington, D.C. 20231

Sir:

This Information Disclosure Statement is being filed before the mailing date of the first Office Action issued on the merits of the above-identified application in accordance with 37 C.F.R. § 1.97(b)(3), and supplements the Information Disclosure Statements previously filed on May 25, 1994, May 15, 1995, and February 16, 1996.

In recognition of Applicant's duty to inform the U.S. Patent and Trademark Office of relevant patents, publications, or other information of which Applicant is aware, Applicant submits herewith copies of the following references relating to *Mycobacterium tuberculosis*.

extracellular proteins which may be material to the examination of the above-identified application.

1. Roche, Paul W., et al. "T-Cell Determinants and Antibody Binding Sites on the Major Mycobacterial Secretory Protein MPB59 of *Mycobacterium bovis*." *Infection and Immunity* 62 (December 1994) 5319-26.
2. Horwitz, Marcus A., et al. "Protective Immunity Against Tuberculosis Induced by Vaccination with Major Extracellular Proteins of *Mycobacterium tuberculosis*." *Proceedings of the National Academy of Science USA* 92 (February 1995) 1530-34.
3. Silver, Richard F., et al. "T-Cell Epitopes of the 30kD Alpha Antigen of *Mycobacterium tuberculosis* BCG: Potential for Use in Vaccines and Diagnosis." *Journal of Cellular Biochemistry — Molecular Mechanisms in Tuberculosis* from the Keystone Symposia on Molecular & Cellular Biology, Supplement 19B, 1995 (February 5 – March 15, 1995) Abstract No. B3-336: 94.
4. Huygen, Kris, et al. "Immunogenicity of a Tuberculosis DNA Vaccine Containing Genes Encoding the Components of the Secreted Antigen 85 Complex." *Journal of Cellular Biochemistry — Molecular Mechanisms in Tuberculosis* from the Keystone Symposia on Molecular & Cellular Biology, Supplement 19B, 1995 (February 5 – March 15, 1995) Abstract No. B3-408.
5. Orme, Ian M., et al. "T Lymphocytes Mediating Protection and Cellular Cytolysis During the Course of *Mycobacterium tuberculosis* Infection." *The Journal of Immunology* 148 (January 1992) 189-96.
6. Young, D. B., et al. "Mycobacterial Protein Antigens: A Compilation." *Molecular Microbiology* 6, no. 2 (1992) 133-45.
7. Lee, Byong-Wha Esther, et al. "Cell-Mediated Immune Responses to the Native 71kD Protein of *Mycobacterium tuberculosis* in Guinea Pigs and Humans." From the Twenty-Seventh U.S.-Japan Leprosy Research Conference, Tuberculosis Research Conference, and Leprosy/Tuberculosis Symposium (August 4-7, 1992).
8. Horwitz, Marcus A., et al. "Progress in the Development of a Subunit Vaccine Against Tuberculosis." From the Twenty-Ninth U.S.-Japan Leprosy Research

Conference, Tuberculosis Research Conference, and Leprosy/Tuberculosis Symposium (August 19-22, 1994).

9. Bloch, Hubert, and William Segal. "Viability and Multiplication of Vaccines in Immunization Against Tuberculosis." *American Review of Tuberculosis* 7 (1955) 228-48.
10. Palmer, C., et al. "Experimental Studies of Vaccination, Allergy, and Immunity in Tuberculosis." *Bulletin of the World Health Organization* 12 (1955) 47-62.
11. Dubos, René J., et al. "Antituberculous Immunity Induced in Mice by Vaccination with Living Cultures of Attenuated Tubercl Bacilli." *Journal of Experimental Medicine* 97 (1953) 207-20.
12. Youmans, G. P. "Acquired Immunity in Tuberculosis." Chap. 8 in *Tuberculosis*. Edited by G. P. Youmans. Philadelphia: The W. B. Saunders Co. (1979).
13. Weiss, David W., and A. Q. Wells. "Immunization with Dead Tubercl Bacilli." *Tubercl* 37 (April 1956) 137-40.
14. Meyer, Sven Nissen. "Animal Studies on Effects of BCG, H37Ra and *Mycobacterium phlei* in Tuberculosis Immunization." *Tubercl* 37 (January - February 1956) 11-22.
15. Wilson, G. S., and A. A. Miles. "Tuberculosis." Chap. 59 in *Topley and Wilson's Principles of Bacteriology and Immunity*. 4th ed. 2 vols. London: Edward Arnold (Publishers) Ltd. (1955).
16. Kubica, George P., and Lawrence G. Wayne, eds. *The Mycobacteria: A Sourcebook*. 2 parts. New York: Marcel Dekker, Inc. 33-57.
17. Infectious Diseases Society of America. *Reviews of Infectious Diseases* 11. Supplement 2. Chicago: The University of Chicago Press (March - April 1989).
  - a) Styblo, Karel. "Overview and Epidemiologic Assessment of the Current Global Tuberculosis Situation with an Emphasis on Control in Developing Countries." S339-46.
  - b) Grosset, Jacques H. "Present Status of Chemotherapy for Tuberculosis." S347-52.

- c) Fine, Paul E. M. "The BCG Story: Lessons from the Past and Implications for the Future." S353-9.
- d) Pio, Antonio. "Impact of Present Control Methods on the Problem of Tuberculosis." S360-5.
- e) Stead, William W. "Pathogenesis of Tuberculosis: Clinical and Epidemiologic Perspective." S366-8.
- f) Dannenberg, Arthur M., Jr. "Immune Mechanisms in the Pathogenesis of Pulmonary Tuberculosis." S369-78.
- g) Quinn, Thomas C. "Interactions of the Human Immunodeficiency Virus and Tuberculosis and the Implications for BCG Vaccination." S379-84.
- h) Smith, Donald W., and Ernst H. Wiegshaus. "What Animal Models Can Teach Us about the Pathogenesis of Tuberculosis in Humans." S385-93.
- i) De Vries, René R. P. "Regulation of T Cell Responsiveness Against Mycobacterial Antigens by HLA Class 2 Immune Response Genes." S400-3.
- j) Jacobs, William R., Jr., et al. "Mycobacteriophage Vector Systems." S404-10.
- k) Patel, Rubina J., et al. "A Cloned DNA Fragment for Identification of *Mycobacterium tuberculosis*." S411-9.
- l) Brennan, Patrick J. "Structure of Mycobacteria: Recent Developments in Defining Cell Wall Carbohydrates and Proteins." S420-30.
- m) Young, Douglas B., and Angela Mehlert. "Serology of Mycobacteria: Characterization of Antigens Recognized by Monoclonal Antibodies." S431-5.
- n) Piessens, Willy F. "Introduction to the Immunology of Tuberculosis." S436-42.
- o) Lamb, Jonathan R., et al. "Identification of Mycobacterial Antigens Recognized by T Lymphocytes." S443-7.
- p) Kaufman, Stefan H. E. "In Vitro Analysis of the Cellular Mechanisms Involved in Immunity to Tuberculosis." S448-54.

- q) Ellner, Jerrold J. and Robert S. Wallis. "Immunologic Aspects of Mycobacterial Infections." S455-9.
- r) Bloom, Barry R. "New Approaches to Vaccine Development." S460-6.
- s) Sensi, Piero. "Approaches to the Development of New Antituberculosis Drugs." S467-70.
- t) Daniel, Thomas M. "Rapid Diagnosis of Tuberculosis: Laboratory Techniques Applicable in Developing Countries." S471-8.
- u) Skamene, Emil. "Genetic Control of Susceptibility to Mycobacterial Infections." S394-9.
- v) Parenti, Francesco. "New Experimental Drugs for the Treatment of Tuberculosis." S479-83.
- w) Wiegeshaus, Ernst H., and Donald W. Smith. "Evaluation of the Protective Potency of New Tuberculosis Vaccines." S484-90.

18. Maugh, Thomas H., 2d. "Promising Tests Reported for New TB Vaccine." *Los Angeles Times*, February 28, 1995, p. 1, col. 3.

Reference Nos. 17(a) to 17(w) are all from the publication listed at No. 17.

Applicant also submits herewith copies of the following references relating to the pathogen *Legionella pneumophila* which may be material to the examination of the above-identified application.

1. Blander, Steven J., and Marcus A. Horwitz. "Vaccination with *Legionella pneumophila* Membranes Induces Cell-mediated and Protective Immunity in a Guinea Pig Model of Legionnaires' Disease." *Journal of Clinical Investigation* 87 (March 1991) 1054-9.
2. Horwitz, Marcus A. "Characterization of Avirulent Mutant *Legionella pneumophila* That Survive but Do Not Multiply within Human Monocytes." *Journal of Experimental Medicine* 166 (November 1987) 1310-28.
3. Berdal, Bjørn P., et al. "Demonstration of Extracellular Chymotrypsin-Like Activity from Various *Legionella* Species." *Journal of Clinical Microbiology* 16 (September 1982) 452-7.

4. Müller, Hans E. "Proteolytic Action of *Legionella pneumophila* on Human Serum Proteins." *Infection and Immunity* 27 (January 1980) 51-3.
5. Horwitz, Marcus A., and Samuel C. Silverstein. "Legionnaires' Disease Bacterium (*Legionella pneumophila*) Multiplies Intracellularly in Human Monocytes." *Journal of Clinical Investigation* 66 (September 1980) 441-50.
6. Horwitz, Marcus A. "Cell-mediated Immunity in Legionnaires' Disease." *Journal of Clinical Investigation* 71 (June 1983) 1686-97.
7. Blander, Steven J., et al. "A Live Avirulent Mutant *Legionella pneumophila* Vaccine Induces Protective Immunity against Lethal Aerosol Challenge." *Journal of Clinical Investigation* 83 (March 1989) 810-5.
8. Blander, Steven J., and Marcus A. Horwitz. "Major Cytoplasmic Membrane Protein of *Legionella pneumophila*, a Genus Common Antigen and Member of the hsp 60 Family of Heat Shock Proteins, Induces Protective Immunity in a Guinea Pig Model of Legionnaires' Disease." *Journal of Clinical Investigation* 91 (February 1993) 717-23.
9. Blander, Steven J., and Marcus A. Horwitz. "Vaccination with the Major Secretory Protein of *Legionella* Induces Humoral and Cell-mediated Immune Responses and Protective Immunity across Different Serogroups of *Legionella pneumophila* and Different Species of *Legionella*." *Journal of Immunology* 147 (July-1991) 285-91.
10. Blander, Steven J., et al. "An Immunoprotective Molecule, the Major Secretory Protein of *Legionella pneumophila*, Is Not a Virulence Factor in a Guinea Pig Model of Legionnaires' Disease." *Journal of Clinical Investigation* 86 (September 1990) 817-24.

All of the above references are also listed on the attached PTO Form-1449.

In filing this Information Disclosure Statement, Applicant notes that none of the references listed above discloses the use of majorly abundant extracellular products to induce protective immunity to subsequent infection by intracellular pathogens.

The filing of this Information Disclosure Statement shall not be construed as a representation that a search has been made, as an admission that the information cited is, or is considered to be, material to patentability, or that no other material information exists.

It is believed that this paper does not require any fee. However, the Commissioner is authorized to charge any fee which may be required in connection with this paper to deposit account No. 16-2230. A duplicate copy of this paper is enclosed for this purpose.

Respectfully submitted,

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